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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,530	09/05/2003	Peter Distefano	13407-020001	9529

26161 7590 01/05/2007
FISH & RICHARDSON PC
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EXAMINER	
LIU, SUE XU	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/656,530	DISTEFANO ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-31 and 36* is/are pending in the application.

4a) Of the above claim(s) *1-24 and 32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-31 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/23;7/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Claim Status

Claim 35 has been cancelled as filed 10/11/06;

Claim 36 has been added as filed 10/11/06;

Claims 1-34 and 36 are currently pending;

Claims 1-24 and 32-34 have been withdrawn;

Claims 25-31 and 36 are being examined in this application.

Election/Restrictions

1. Applicant's election of Group VI (Claims 25-31) in the reply filed on 10/11/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicants added a new Claim 36, which is dependent on Claim 25, and thus is grouped with Group VI invention.

3. Claims 1-24 and 32-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/11/06.

4. Applicant's election with traverse of the following species in the reply filed on 10/11/06 is acknowledged:

A.) Ghrelin receptor as the GH/IGF-1 axis component;

B.) A non-human animal model to be contacted by a compound;

C.) A small organic molecule as the test compound;

D.) A metabolic disorder as a disorder;

E.) A cell surface receptor;

F.) The species requirement of "A single specific and defined number of nucleotide mutations per nucleic acid sequence" as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

G.) An antagonist;

H.) A cell-based assay;

I.) A human subject as a subject;

J.) The species requirement of "A single selection of an age-associated parameter" as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

K.) The species requirement of "A single selection of a direct antagonist..." as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

The traversal is on the ground(s) that there would be no serious burden to search all the different species. This is not found persuasive because the different species are distinct, and would require separate searches in both the patent and non-patent databases. For example, the different components of the GH/IGF-1 axis are at least different proteins that do not share common core structure, function, and/or property. Search of one protein component of the axis may not be extensive over another component of the axis. In addition, species selection only

serves as a starting point for examination. That is if the selected species is allowable, then the examination of the next species in the list will be conducted.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Sequence Rule Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) below:

Applicants are respectively directed to the attached "Notice to Comply" for further details on compliance with the Sequence Rule. Applicants are requested to submit sequence listings and amend the instant specification accordingly.

Priority

6. This application claims priority to the following U.S. Provisional Patent Application Nos. 60/487,308, filed on 7/14/2003, 60/487,344, filed on 07/14/2003, and 60/408,560, filed on 09/06/2002.

Specification

7. The disclosure is objected to because of the following informalities: On page 39 of the instant specification, the disclosure recites "FIG. 6 is a schematic of the..." (p. 39, para 6), however, the instant application only contains total of three drawings.

Appropriate correction is required.

In addition, the specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

9. Claims 25-31 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite a method identifying a GH/IGF-1 axis antagonist or partial agonist, the method comprising

a) providing a test compound that is obtained by chemically modifying an agonist of GH/IGF-1 axis component or that is selected for structural similarity to an agonist of GH/IGF-1 axis component; and

b) evaluating a property of a GH/IGF-1 axis component in vitro, in a cell, or in an organism in the presence of the test compound, wherein ability of the test compound to modulate the property of the GH/IGF- 1 axis component identifies the test compound as a GH/IGF- 1 axis antagonist.

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli

Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

The instant claims are drawn to a method that require "a test compound", and "GH/IGF-1 axis component". Without providing structural limitation for the claimed "test compound" and "GH/IGF-1 axis component", the claims are drawn to a genus of "test compound" that can be any compound, and a genus of GH/IGF-1 axis component that can be any component of the GH/IGF-1 axis. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of "test compounds" and the genus of "GH/IGF-1 axis component". In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of compounds and genus of GH/IGF-1 axis components.

Although the instant specification lists general examples of compounds (p. 50+), the instant specification does not provide common structural limitation for the entire genus of

compounds, and compounds that are structural similar thereto. In addition, the instant specification does not specifically define the limit for the term "structural similar", the claimed test compounds could be any compound.

Similarly, the instant specification lists several "GH/IGF-1 axis components", however, the instant specification does not provided a common structure to demonstrate the possession of all the members of the axis.

The art also does not teach all possible compounds that can be made and administered to any organism. Further, the art also does not teach all possible components for the GH/IGF-1 axis, which comprise diverse biological molecules such as different proteins and hormones as disclosed by the instant specification (p. 40). It is not known in the art that all of the components (all the different proteins and/or hormones) are known for the axis.

Therefore, applicants are not in possession of methods that can test any compounds in any organism that can modulate any component of the GH/IGF-1 axis. Applicant's claimed scope represents only an invitation to experiment regarding possible compounds that can be tested with any components of the GH/IGF-1 axis.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 25-31 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 recites the phrase "structural similarity", which is a relative term and rendering the claim indefinite. The instant specification does not specifically define the term "structural similarity". It is not clear on what basis and/or parameters the compounds are to share structural similarities. In addition, it is not clear the degree of similarity is required for the selected compound to be shared with an "agonist". Further, the claim (25) also does not clearly recite how a compound is to be selected base on "structural similarity".

Claim 29 recites "wherein a cohort of adult organism are treated and evaluated", which is unclear as to how the adult organisms are treated and evaluated.

Claim 30 recites the phrase "decreased levels", which is indefinite because it's a relative term. Neither the instant specification nor the claims define the specific levels or relative levels the tested components (e.g. GH and/or IGF-1) have to decrease for "the test compound" to be "a modulator".

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

13. Claims 25-31 and 36 are rejected under **35 U.S.C. 102(b)** as being anticipated by Smith et al (Endocrine Reviews. Vol. 18(5): 621-645; Oct., 1997).

The instant claims recite a method identifying a GH/IGF-1 axis antagonist or partial agonist, the method comprising

a) providing a test compound that is obtained by chemically modifying an agonist of GH/IGF-1 axis component or that is selected for structural similarity to an agonist of GH/IGF-1 axis component; and

b) evaluating a property of a GH/IGF-1 axis component in vitro, in a cell, or in an organism in the presence of the test compound, wherein ability of the test compound to modulate the property of the GH/IGF- 1 axis component identifies the test compound as a GH/IGF- 1 axis antagonist.

Smith et al, throughout the publication, teach various compounds (peptidomimetics) that can be used for regulation of growth hormone (GH) secretion (see entire document). The reference teaches various compounds (peptides or peptidomimetics) that can modulate activities of at least the GH and GHSR (Ghrelin receptor) in the GH/IGF-1 axis (pp. 621-627; especially, p. 624. right col., p. 625, left col., and p. 630, right col.). The MK-0677 (p. 625, Figure 4), for example, reads on the test compound of the claimed test compound of **clm 25**. The MK-0677 is a derivative of an antagonist or an agonist (p. 624, right col., para 2 and p. 625, left col., para 2), which reads on the chemically modifying an agonist of the GH/IGF-I component of **clm 25**. The reference also teaches pituitary cell based assay, and GH hormone assay in rats and dogs (p. 625, Left-right col., bridging para), which reads on step b) of **clm 25**, and cell-based assay of **clms 26**

and 27. The reference specifically teaches that the beagles has elevated GH and IGF-I levels after administering MK-0677 (p. 625, left-right col., bridging lines), and thus the beagles has normal IGF-1 levels prior to administering as recited in **clm 28**. The reference's teaching (p. 625, Left-right col., bridging para) also reads on a cohort of adult animals as recited in **clm 29**, and the evaluating step of **clm 31**. The reference teaches administering oral dosage to dogs or rats (p. 625, left col., para 2, p. 635, left-right cols.), which reads on the pharmaceutically acceptable carrier of **clm 36**. The reference also teaches particular dosing regimens of MK-0677 for dogs lowered IGF-I to basal levels (p. 635, right col.) and lowered GH level to basal levels as well (p. 636, left col., para 1), which reads on the decreased levels of GH and/or IGF-1 of **clm 30**.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON EPPERSON
PRIMARY EXAMINER

SL
Art Unit 1639
12/18/2006

NOTEs-10/656530

Rejection:

See p. 50 of the spec. for reference on compounds that decrease GH. For treating acromegaly, which is characterized by excess GH.

Spec.

Growth hormone—p. 39.

Organismal assay---p. 70, specifically says use non-human.

Ghrelin GHS receptor ---p. 58, top.

Seq Compliance: pg. 53 of spec. has sequence but no sequence listing.

ODP: searched; none;

References:

Reviews:

Scarth et al (in Folder): Modulation ofhte growth hormone-insulin-like growth factor (GH-IGF) axis by pharmaceutical, nutraceutical and environmental xenobiotics: AN emerging role for xenobiotic-metabolizing enzymes and the transcription factors regulating their expression.

Rincon (in folder): Experimental Gerontology. Vol. 40: 873-877; 2005; GH/IGF. General about GH/IGF; last sections; citation p. 877, Khan et al. (maybe useful).

Hosoda et al (J. pharmacological. Sciences. Vol. 100: 398-410; 2006); Ghrelin. Maybe 102b; talks about effects of Ghrenlin on GH, and other hormones. (Also human data: p. 402, right col., 2nd para).

Bartke (in IDS): general review;

Patchett et al. (cited in IDS; also in folder): PNAS. 1995; vol. 92: 7001-7005; Can be 102b: MK-0677, which increases GH and IGF levels.

Muccioli et al. (in folder): Journal of endocrinology. Vol. 157: 99-106; 1998; Specific receptors for synthetic GH secretagogues in the human brain and pituitary gland. Binding peptides to GHS receptors. (maybe 103 or smthing).

Kojima et al. (in folder); Trends in endocrinology and metabolism. Vol. 12(3): 118-126); 4/2001. Ghrelin: discovery of the natural endogenous ligand for the growth hormone secretagogue receptor. Not really useful.

Baldelli et al (IDS): GH secretagogues;

Kopchick et al (IDS): mostly GH and GH receptor; maybe 102b: develping a GH antagonists using mice.

Holst et al. (Journal of clinical investigation. Vol. 116(3): 637-641. 2006; Ghrelin related to obesity.

Tullin (in folder). Endocrinology. Vol. 141(9): 3397-3402. 2000; Adenosine as an agonist for growth hormone secretagogue receptor. Using cell based assay. (rat).

Nagamine et al. (Journal of endocrinology. Vol. 171: 481-489. 201). A new orally active growth hormone secretagogue. (Audlt male rats).

Blum et al. (IDS): in vitro system (not cell based assay) to study inhibition of autophophorylation of IGF receptor.

WO 02/072780: 102e date--- IGF antagonist peptides

WO 02/102804: 102e date--- cycloliganans useful fro treatment of IGF-1R dependent diseases.

Carter et al. (Trends in genetics. Vol. 18(6): 295-301) in IDS: mammalian models (using mice).

Notice to Comply	Application No. 10656530	Applicant(s) DISTEFANO ET AL.
	Examiner Sue Liu	Art Unit 1639

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application.**

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
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